

**REMARKS**

This Reply is responsive to the Office Action dated July 17, 2002. Entry of the amendments and remarks submitted herein and reconsideration of the claimed subject matter pursuant to 37 CFR §1.112 is respectfully requested.

**I. Status of the Claims**

At the outset, Applicants acknowledge with appreciation the rejoinder of claims 12, 13 and 17 with the elected invention. Accordingly, claims 1, 2, 4-8, 11-18, 23-31, 33 and 35-50 were under examination in this application at the time of the Office Action dated July 17, 2002. Claims 3, 19-22, 32 and 34 have been withdrawn from consideration. As a result of this amendment, claim 50 has been canceled, and new claim 51 has been added. Accordingly, claims 1, 2, 4-8, 11-18, 23-31, 33, 35-49 and 51 are now pending and under examination.

**II. Amendments to the Claims**

Claim 50 was canceled above and claim 33 was amended to correct a minor typographical error included in the previous amendment. Claim 40 was amended to refer to generically to a GAL4 driver and UAS-*dpp*. Support for this amendment may be found on page 18, lines 22-23, and on page 18, line 33. In addition, new claim 51 was added indicating that expression of the *dpp* nucleic acid can be provided by mating *Drosophila* lines expressing the GAL4 driver and UAS-*dpp*. Support for this new claim may be found on page 27, lines 1-2. No prohibited new matter was added by way of these amendments.

### III. Office Action

Claim 33 was objected to because the only two steps recited (as depicted in the appendix of the amendment filed February 19, 2002), were labeled (c) and (d) rather than (a) and (b). The claim has been amended above to relabel the steps as (a) and (b) as suggested in the Office Action. Accordingly, this objection may now be withdrawn.

#### A. Rejection under 35 U.S.C. §112, first paragraph

Claim 40 was rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification so as to enable one to make and/or use the invention. Specifically, since claim 40 refers to hsp70-GAL4 and UAS-*dpp* vectors by name, the Office Action has inquired as to the public availability of the vectors.

Applicants respectfully note that claim 40 has been amended to refer more generically to a GAL4 driver. The term UAS-*dpp* in the claim refers generically to any UAS-*dpp* construct and not to any specific construct required to practice the invention. The GAL4-UAS system was known and used by many in the art prior to the filing date of the present invention and therefore Applicants need not attest to the public availability of this system. In any case, all *Drosophila* stocks employed in the specification may be obtained from the Bloomington Stock Center, an NIH-approved stock center at Indiana University (see page 26, lines 9-13 of the specification). Reconsideration and withdrawal of the rejection under §112, first paragraph is respectfully requested.

**Rejection under 35 U.S.C. §112, second paragraph**

Claims 46 and 50 were rejected under 35 U.S.C. §112, second paragraph for alleged indefiniteness, because it is unclear how claim 50 further limits claim 46.

Without necessarily agreeing with the rejection and in an effort to advance prosecution, Applicants have canceled claim 50 above. Accordingly, the rejection under §112, second paragraph may now be withdrawn.

**B. Rejections under 35 U.S.C. §102**

Claims 1, 2, 4-8, 11-18, 23, 24, 28-31, 33, 35-39 and 41-50 remain rejected under 35 U.S.C. §102(b) as being anticipated by either Twombly *et al.* or Forbes *et al.*

Essentially, in the absence of some evidence that the transgenic *Drosophila* disclosed by these references do not exhibit an increased abundance of stem cells, the Office Action asserts that the transgenic *Drosophila* disclosed therein would inherently produce an increased abundance of stem cells since they contain a *dpp* transgene. Further, in the case of Forbes *et al.*, the Office Action asserts that the increase in germline cells observed by Forbes *et al.* meets the limitations of the instant claims. Applicants respectfully traverse the rejections.

Submitted concurrently herewith is a declaration pursuant to 37 CFR §1.132 executed by Dr. Allan Spradling, a coinventor of the present application and a coauthor of the Forbes *et al.* reference. As Dr. Spradling avows in his declaration, his laboratory examined the *Drosophila* reported in the Forbes *et al.* paper for an increase in the abundance of germline stem but no such increase was observed (see paragraphs 4 and 5 of the declaration). Further, the increased "germline cells" mentioned in the Office

Action were not germline stem cells but rather differentiated daughter cells, which are physically distinguishable from germline stem cells (*i.e.*, by differences in protein expression). Indeed, as described in Example 4 of the specification, stem cells are lost through differentiation (page 20, lines 18-19). Therefore, an increase in differentiated daughter cells is akin to a reduction in germline stem cells rather than an increase as claimed (see also paragraph 5 of the declaration).

With regard to Twombly *et al.*, Dr. Spradling explains in his declaration how no increase in the number of germline stem cells could have occurred in this study given the particular vectors employed and the specific heat shock protocol used (paragraphs 7 and 8 of declaration). Furthermore, as Dr. Spradling explains, the focus in Twombly *et al.* on later developmental stages is evidence that an increase in germline stem cells did not occur because if the stem cell number had been significantly increased, these late developmental stages would not have been present. According to Dr. Spradling, in his experience, the production of later follicles is completely blocked before significant numbers of stem cells accumulate. Thus, the fact that Twombly *et al.* observed and studied older follicles in their experiments confirms that there was not a significant block of stem cell development sufficient to result in an increased number of stem cells (see paragraph 7 of the declaration).

Thus, according to the declaration by Dr. Spradling, no increase in the number of germline stem cells occurred in the experiments reported in Twombly *et al.* or Forbes *et al.* Accordingly, neither reference teaches providing expression of a dpp nucleic acid so as to result in an increase in the abundance of germline stem cells as claimed.

Reconsideration and withdrawal of the rejections under §102(b) based on the Twombly *et al.* and Forbes *et al.* references is respectfully requested.

**C. Rejection under 35 U.S.C. §103(a)**

Claims 1 and 25-27 were rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over either Forbes *et al.* or Twombly *et al.* and Lin *et al.* According to the Office Action, the Twombly and Forbes references are relied on for the reasons discussed above. Lin *et al.* is provided only to teach that at the time of filing transfer of germline stem cells into a host *Drosophila* was routine in the art and used to study the effects on germinal cells. Thus, according to the Office Action, it would have been *prima facie* obvious for one of ordinary skill in the art at the time of the claimed invention to use the methods of germinal cell transfer as taught by Lin *et al.* to implant the stimulated germline stem cells of Forbes *et al.* or Twombly *et al.* to examine the influence of transgene behavior on oogenesis. Applicants respectfully traverse the rejection.

As discussed above and described in more detail in the §1.132 declaration by Dr. Allan Spradling submitted herewith, neither Forbes *et al.* nor Twombly *et al.* teaches, either explicitly or inherently, an increase in the abundance of germline stem cells as recited in claim 1. Lin *et al.* does not make up for this deficiency because, as acknowledged in the Office Action, Lin *et al.* is only relied on for teaching that methods of germinal cell transfer in *Drosophila* were routine at the time the invention was made. Accordingly, the combination of Forbes *et al.* or Twombly *et al.* and Lin *et al.* does not render obvious the transfer of germline stem cells from a host that produces an increased

abundance of germline stem cells according to the claimed method. Reconsideration and withdrawal of the rejection under §103(a) is respectfully requested.

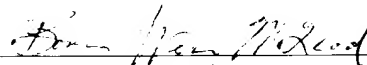
This reply is fully responsive to the Office Action dated July 17, 2002. Therefore, a Notice of Allowance is next in order and is respectfully requested.

Except for issue fees payable under 37 CFR §1.18, the commissioner is hereby authorized by this paper to charge any additional fees during the pendency of this application including fees due under 37 CFR §1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 CFR §1.136(a)(3).

If the Examiner has any further questions relating to this Reply or to the application in general, he is respectfully requested to contact the undersigned by telephone so that allowance of the present application may be expedited.

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

By:   
Bonnie Weiss McLeod  
Reg. No. 43,255

Dated: January 16, 2003  
**CUSTOMER NO.: 009629**  
**MORGAN, LEWIS & BOCKIUS LLP**  
1111 Pennsylvania Avenue, N.W.  
Washington, D.C. 20004  
Telephone: 202-739-3000  
Facsimile: 202-739-3001

**APPENDIX**

The following amendments were entered above:

IN THE CLAIMS:

33. (Twice Amended) A method for maintaining *Drosophila* stem cells *in vivo* comprising:

[(c)] (a) providing a population comprised of stem cells, and

[(d)] (b) stimulating a *decapentaplegic* (*dpp*) signaling pathway in at least one stem cell in said population by providing expression of a nucleic acid encoding Dpp,

such that there is an increase in abundance of undifferentiated stem cells in said population as compared to a population of stem cells which has not been stimulated.

40. (Amended) A method according to claim 1, wherein said Dpp is ectopically expressed in germarium of said host *Drosophila* using [hsp70-GAL4] a GAL4 driver and UAS-*dpp*.